INTERNATIONAL SEARCH REPORT

Inte l Application No
PCT/GB2004/003236

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, BIOSIS, WPI Data, EMBASE, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NISHIZATO YOHEI ET AL: "Polymorphisms of OATP-C (SLC21A6) and OAT3 (SLC22A8) genes: consequences for pravastatin pharmacokinetics." CLINICAL PHARMACOLOGY AND THERAPEUTICS. JUN 2003, vol. 73, no. 6, June 2003 (2003-06), pages 554-565, XP002306135 ISSN: 0009-9236 cited in the application	1,4-12, 15-21
A	abstract page 560, right-hand column - page 561 page 562 - page 563 tables I-VI	2,3,13, 14

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance
"E" earlier document but published on or after the international filing date
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
"O" document referring to an oral disclosure, use, exhibition or other means
"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 March 2005	04. 04. 2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax (+31-70) 340-3016	Madlener, M

Form PCT/ISA/210 (second sheet) (January 2004)

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Inter al Application No
PCT/GB2004/003236

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	TIRONA ROMMEL G ET AL: "Polymorphisms in OATP-C. Identification of multiple allelic variants associated with altered transport activity among European- and African-Americans" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 276, no. 38, 21 September 2001 (2001-09-21), pages 35669-35675, XP002306136 ISSN: 0021-9258 cited in the application	1,4-12, 15-21
A	page 35672 - page 35673 figures 1-4 tables I-II abstract	2,3,13, 14
A	US 2002/090622 A1 (DUDLEY ADAM JESTON ET AL) 11 July 2002 (2002-07-11) abstract paragraph '0075! - paragraph '0098! claims 1-12	1-21
A	NOZAWA TAKASHI ET AL: "Genetic polymorphisms of human organic anion transporters OATP-C (SLC21A6) and OATP-B (SLC21A9): Allele frequencies in the Japanese population and functional analysis" JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, vol. 302, no. 2, August 2002 (2002-08), pages 804-813, XP002306137 ISSN: 0022-3565 the whole document	1-21
A	TIRONA R G ET AL: "Pharmacogenomics of organic anion-transporting polypeptides (OATP)" ADVANCED DRUG DELIVERY REVIEWS, AMSTERDAM, NL, vol. 54, no. 10, 18 November 2002 (2002-11-18), pages 1343-1352, XP002245997 ISSN: 0169-409X the whole document	1-21

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Inter l Application No
PCT/GB2004/003236

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	IGEL M ET AL: "PHARMACOLOGY OF 3-HYDROXY-3-METHYLGLUTARYL-COENZYME A REDUCTASE INHIBITORS (STATINS), INCLUDING ROSUVASTATIN AND PITAVASTATIN" JOURNAL OF CLINICAL PHARMACOLOGY, LIPPINCOTT CO, HAGERSTOWN, MD, US, vol. 42, no. 8, August 2002 (2002-08), pages 835-845, XP008016576 ISSN: 0091-2700 cited in the application the whole document	1-21
A	KÖNIG J ET AL: "A novel human organic anion transporting polypeptide localized to the basolateral hepatocyte membrane." AMERICAN JOURNAL OF PHYSIOLOGY. GASTROINTESTINAL AND LIVER PHYSIOLOGY. JAN 2000, vol. 278, no. 1, January 2000 (2000-01), pages G156-G164, XP002191047 ISSN: 0193-1857 the whole document	1-21
A	TAMAI I ET AL: "MOLECULAR IDENTIFICATION AND CHARACTERIZATION OF NOVEL MEMBERS OF THE HUMAN ORGANIC ANION TRANSPORTER (OATP) FAMILY" BIOCHIMICA ET BIOPHYSICA ACTA, AMSTERDAM, NL, vol. 273, no. 1, 2000, pages 251-260, XP000941538 ISSN: 0006-3002 cited in the application the whole document	1-21
A	JUNG DIANA ET AL: "Characterization of the human OATP-C (SLC21A6) gene promoter and regulation of liver-specific OATP genes by hepatocyte nuclear factor 1alpha" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 276, no. 40, 5 October 2001 (2001-10-05), pages 37206-37214, XP002306138 ISSN: 0021-9258 the whole document	1-21
A	WEISS K M ET AL: "Linkage disequilibrium and the mapping of complex human traits" TRENDS IN GENETICS, ELSEVIER, AMSTERDAM, NL, vol. 18, no. 1, 1 January 2002 (2002-01-01), pages 19-24, XP004326531 ISSN: 0168-9525 the whole document	1-21

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INTERNATIONAL SEARCH REPORT

Inter al Application No
PCT/GB2004/003236

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	MWINYI JESSICA ET AL: "Evidence for inverse effects of OATP-C (SLC21A6) *5 and *1b haplotypes on pravastatin kinetics" CLINICAL PHARMACOLOGY & THERAPEUTICS, vol. 75, no. 5, May 2004 (2004-05), pages 415-421, XP002306139 ISSN: 0009-9236 cited in the application	1,4-12, 15-21
P,A	abstract	2,3,13, 14
P,X	NIEMI MIKKO ET AL: "High plasma pravastatin concentrations are associated with single nucleotide polymorphisms and haplotypes of organic anion transporting polypeptide-C (OATP-C, SLCO1B1)" PHARMACOGENETICS, vol. 14, no. 7, July 2004 (2004-07), pages 429-440, XP009039924 ISSN: 0960-314X cited in the application	1,4-12, 15-21
P,A	abstract	2,3,13, 14
P,X	KIM RICHARD B: "3-Hydroxy-3-methylglutaryl-coenzyme A reductase inhibitors (statins) and genetic variability (single nucleotide polymorphisms) in a hepatic drug uptake transporter: what's it all about?" CLINICAL PHARMACOLOGY AND THERAPEUTICS. MAY 2004, vol. 75, no. 5, May 2004 (2004-05), pages 381-385, XP009039939 ISSN: 0009-9236	1,4-12, 15-21
P,A	page 383	2,3,13, 14
A	ANONYMOUS: "OATP-C: SLCO1B1" GENECARDS, 'Online! XP002317182 Retrieved from the Internet: URL:http://genecards.weizmann.ac.il/cgi-bin/cards/carddisp?SLCO1B1&search=oatp-c&suff=txt> the whole document -& ANONYMOUS: "SNP linked to Gene (geneID: 10599)" SINGLE NUCLEOTIDE POLYMORPHISM, 'Online! XP002320267 Retrieved from the Internet: URL:http://www.ncbi.nlm.nih.gov/SNP//snp_ref.cgi?locusId=10599>	1-21

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INTERNATIONAL SEARCH REPORT

Int al Application No
PCT/GB2004/003236

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	DATABASE EMBL 'Online! 15 March 2000 (2000-03-15), "Homo sapiens chromosome 11 clone RP11-484D2, WORKING DRAFT SEQUENCE, 22 unordered pieces." XP002317183 retrieved from EBI accession no. EM_PRO:AC025552 Database accession no. AC025552 the whole document	1-21
A	CALAFELL F ET AL: "HAPLOTYPE EVOLUTION AND LINKAGE DISEQUILIBRIUM) A SIMULATION STUDY" HUMAN HEREDITY, KARGER, BASEL, CH, vol. 51, no. 1/2, October 2000 (2000-10), pages 85-96, XP001107179 ISSN: 0001-5652 the whole document	1-21
A	STEPHENS J C ET AL: "Haplotype variation and linkage disequilibrium in 313 human genes" SCIENCE, AMERICAN ASSOCIATION FOR THE ADVANCEMENT OF SCIENCE,, US, vol. 293, no. 5529, 20 July 2001 (2001-07-20), pages 489-493, XP002213211 ISSN: 0036-8075 the whole document	1-21
A	KRUGLYAK L: "Prospects for whole-genome linkage disequilibrium mapping of common disease genes" NATURE GENETICS, NATURE AMERICA, NEW YORK, US, vol. 22, June 1999 (1999-06), pages 139-144, XP002958585 ISSN: 1061-4036 the whole document	1-21
A	JORDE L B: "Linkage disequilibrium and the search for complex disease genes" GENOME RESEARCH, COLD SPRING HARBOR LABORATORY PRESS, US, vol. 10, no. 10, October 2000 (2000-10), pages 1435-1444, XP002224534 ISSN: 1088-9051 the whole document	1-21

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INTERNATIONAL SEARCH REPORT

Inter al Application No
PCT/GB2004/003236

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	TOIVONEN H T T ET AL: "DATA MINING APPLIED TO LINKAGE DISEQUILIBRIUM MAPPING" AMERICAN JOURNAL OF HUMAN GENETICS, AMERICAN SOCIETY OF HUMAN GENETICS, CHICAGO, IL, US, vol. 67, no. 1, July 2000 (2000-07), pages 133-145, XP000995225 ISSN: 0002-9297 the whole document	1-21
A	AKEY J ET AL: "Haplotypes vs single marker linkage disequilibrium tests: what do we do gain?" EUROPEAN JOURNAL OF HUMAN GENETICS, KARGER, BASEL, CH, vol. 9, no. 4, April 2001 (2001-04), pages 291-300, XP002964641 ISSN: 1018-4813 the whole document	1-21
A	REICH D E ET AL: "LINKAGE DISEQUILIBRIUM IN THE HUMAN GENOME" NATURE, MACMILLAN JOURNALS LTD. LONDON, GB, vol. 411, no. 6834, 10 May 2001 (2001-05-10), pages 199-204, XP001026202 ISSN: 0028-0836 the whole document	1-21
A	SHUANGLIN ZHANG ET AL: "Linkage disequilibrium mapping with genotype data" GENETIC EPIDEMIOLOGY, LISS, NEW YORK, NY,, US, vol. 22, 2002, pages 66-77, XP002903060 ISSN: 0741-0395 the whole document	1-21

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2004/003236

Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

   a. type of material

   [X] a sequence listing

   [ ] table(s) related to the sequence listing

   b. format of material

   [X] in written format

   [X] in computer readable form

   c. time of filing/furnishing

   [ ] contained in the international application as filed

   [ ] filed together with the international application in computer readable form

   [X] furnished subsequently to this Authority for the purpose of search

2. [ ] In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2004/003236

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. ☒ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

1, 3, 11-21 (completely); 2, 4-10 (partially) (inventions 1, 3 and 9)

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

☐ The additional search fees were accompanied by the applicant's protest.

☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1, 4-12, 15-21 (partially)

Use of the Val174Ala polymorphism in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

2. claims: 1-10, 15-21 (partially)

Use of an allele of the -26A>G polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

3. claims: 1-10, 15-21 (partially); 13-14 (completely)

Use of an allele of the -118A>C polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

4. claims: 1-10, 15-21 (partially)

Use of an allele of the -309T>C polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

5. claims: 1-10, 15-21 (partially)

Use of an allele of the -878A>G polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

6. claims: 1-10, 15-21 (partially)

Use of an allele of the -903C>T polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

7. claims: 1-10, 15-21 (partially)

Use of an allele of the -1054G>T polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

8. claims: 1-10, 15-21 (partially)

Use of an allele of the -1215T>A polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

9. claims: 1-10, 15-21 (partially)

Use of an allele of the -1558T>C polymorphism of SEQ.ID.NO.2, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

10. claims: 1-10, 15-21 (partially)

Use of an allele of the T2122G polymorphism of SEQ.ID.NO.3, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

11. claims: 1-10, 15-21 (partially)

Use of an allele of the C2158T polymorphism of SEQ.ID.NO.3, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

12. claims: 1-10, 15-21 (partially)

Use of an allele of the A2525C polymorphism of SEQ.ID.NO.3, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

---

13. claims: 1-10, 15-21 (partially)

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Use of an allele of the G2651A polymorphism of SEQ.ID.NO.3, which is in linkage disequilibrium with the Val174Ala polymorphism, in human OATP-C in statin therapy, based on an effect of said polymorphism on statin pharmacokinetics in humans.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/GB2004/003236

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2002090622 A1	11-07-2002	US 2004235006 A1	25-11-2004
		EP 1186672 A2	13-03-2002
		JP 2002330758 A	19-11-2002

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